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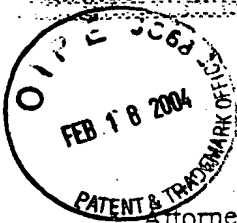
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Attorney Docket No. 9310.22CX

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

In re: Goudsmit et al.

Application Serial No: 09/463,352

Group Art Unit: 1655

Filed: January 21, 2000

Examiner: B. Sisson

For: *NUCLEIC ACID SEQUENCES THAT CAN BE USED AS PRIMERS AND PROBES IN  
THE AMPLICATION AND DETECTION OF ALL SUBTYPES OF HIV-1*

MAIL STOP RCE

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

DECLARATION OF JAAP GOUDSMIT,  
PIETER OUDSHOORN, SUZANNE JURRIAANS  
AND VLADIMIR VLADIMIROVICH LUKASHOV  
UNDER 37 C.F.R. § 1.131

Sir:

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Pieter Oudshoorn

\_\_\_\_\_  
Suzanne Jurriaans

\_\_\_\_\_  
Vladimir Vladimirovich Lukashov

\_\_\_\_\_  
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*Oct 1st 2003*  
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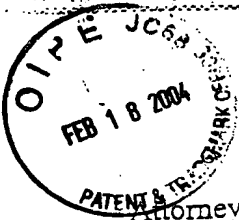
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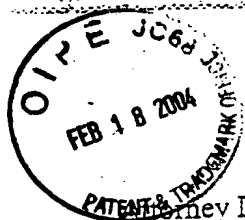
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October 3, 2003  
Date

Pieter Oudshoorn

Date \_\_\_\_\_

**Suzanne Jurriaans**

Date \_\_\_\_\_

Vladimir Vladimirovich Lukashov

Date \_\_\_\_\_



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R&amp;D

Boxtel The Netherlands

Diagnostics

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## Author:

Department	Name	Date	Signature
NDU	F. Jacobs		

## Approval:

Function	Name	Date	Signature
Groupleader	P. Oudshoorn		

To be returned to R&amp;D secretary before submitting for final approval

## Final authorization:

Function	Name	Date	Signature
NDU manager	C. v. Buul		

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## 2. Materials and methods

### 2.1 Design of primers and probes.

The oligonucleotide sequences are respectively:

P1.1: *aat tct aat acg act cac tat agg gAG AGG GGC GCC ACT GCT AGA GA*  
P1.2: *aat tct aat acg act cac tat agg gAG AGG TTC GGG CGC CAC TGC TAG A*  
U5 end: *aat tct aat acg act cac tat agg gCGGGCGCCACTGCTA*  
P2.1: CTG CTT AAA GCC TCA ATA AA  
P2.2: CTC AAT AAA GCT TGC CTT GA

To perform ECL detection one biotin probe and two different detection probes were designed with the following sequences:

HIV-1 LTR-bio: TCT GGT AAC TAG AGA TCC CTC  
HIV-LTR-AMN1: TAG TGT GTG CCC GTC TGT.  
HIV-LTR-AMN2: AGT GTG TGC CCG TCT GTT.

## 2.2

### Evaluation and optimization of the primers and probes.

The primers were tested directly in the amplification in the combinations P1.1/P2.1, P1.1/P2.2, P1.2/P2.1, P1.2/P2.2 and U5-end/P2.2 on in vitro *LTR* RNA and on Scott Layne RNA (subtype B, stock solution of  $5.5 \times 10^9$  copies RNA/ml). The input of the RNA was  $10^4$  copies. The amplifications were examined on a 2% agarose gel and then blotted in 1 hour on zeta probe and cross-linked with UV. The blot was hybridized with the biotin probe (3  $\mu$ M) by incubating the blot for 4 hours at 50°C. After hybridization the blot was washed two times for 5 minutes with 3\*SSC/1%SDS solution at 50°C and one time for 10 minutes with 2\*SSPE/0.1%SDS solution at RT. After this the blot was incubated for 30 minutes with 2  $\mu$ l streptavidine/HRP solution (500 U/ml, Enhanced ChemiLuminiscence detection kit from Amersham) in 10 ml 5\*SSPE/0.5%SDS. The blot was again washed two times for 5 minutes in 2\*SSPE/0.1%SDS solution and one time for 10 minutes in 2\*SSPE solution. The blot was dried between tissues and developed with the development solutions from the enhanced chemiluminiscence kit (Amersham). The blot was wrapped in Saran wrap and a film was placed on the blot for a couple of seconds. The film was developed according to the standard procedures.



### 3.2 Evaluation of selected primers.

*Figure 3. Detection of the amplimers on blot.*

The primersets used were: nr 1: P1.1-P2.1, nr 2: P1.1-P2.2, nr 3: P1.2-P2.1, nr 4: P1.2-P2.2, nr 5: U5 end-5'LTRSph1. The RNA used as input were: A: in vitro RNA  $10^4$  copies per input, B: Scott Layne RNA  $10^4$  copies per input, C: No Templates.

